The present invention provides a coated metal surface on a solid support, wherein the coating consists of a protein layer that is firmly attached to the metal surface, the protein layer being coupled to linker molecules that are bound to low molecular weight antigens, wherein the linker molecules contain between the functional groups, via which they are coupled to the protein layer respectively bound to the antigen, an aliphatic hydrocarbon chain of 1, 2, or 3 carbon atoms. The coated surface provided by the present invention is for use in a displacement reaction where the affinity of an antibody to the antigen that is bound on the coated surface has to be lower than the affinity to the antigen in the test solution. In this regard, see especially claims 12 and 16-18 which contain additional limitations which cannot be ignored. More than three carbon atoms in the aliphatic chain results in a stronger affinity between the antibody and the on the coating bound antigen, which does not promote a displacement reaction. The affinity of the antibody to the antigen bound on the coated surface has to be weaker than that to the antigen in the test solution, otherwise a sufficient displacement of antibodies bound to antigens on the coated surface by antigens in the test solution will not take place, thus resulting in no detection/determination or very poor detection/determination of the antigens in the test solution.

Applicants most respectfully submit that the overall teachings of the reference must be considered in evaluating the patentability of the claimed subject matter and must take into consideration the level of one of ordinary skill in the art to which the invention pertains. Even in view of KSR, there is a requirement for a clear articulation of the reason for the obviousness conclusion and this must take into consideration the teachings of the reference as a whole. With respect to Miura et al., as already pointed out earlier and the Examiner has admitted, this reference does not disclose a linker with 1, 2 or 3 carbon atoms between the functional groups as required by the presently claimed invention. Moreover, as stated in the abstract, the medical substance, i.e., antigen as an object to be measured, is fixed to the surface of the thin metal film and this does not suggest the displacement aspect of the claimed subject matter.

The Jacobs et al. reference discloses a protein layer on a substrate surface and a linker with functional groups (NHS-Y-NHS), however, as also admitted by the Examiner, there is no mention of what the length of Y is or for that matter if the Y is an aliphatic hydrocarbon chain at all. In addition, there is whatsoever no mention of the significance of the affinity between the antibodies, the antigens bound on the coated surface and the antigens in the test solution or displacement reactions. On the contrary, the impression that a skilled person in the art gets when reading the disclosure of Jacobs is that there it is implicitly indicated that the affinity of the antibody to the antigen bound on the protein layer has to be strong in order to achieve the desired test results.

The Tao et al. reference does not mention anywhere implicit or explicit anything about either affinity relations/problems between the target analytes and the capture ligands or displacement reactions. Moreover, Tao et al. does not teach or suggest a coated metal surface according to the present invention where the coating consists of a protein layer firmly attached on a metal surface and the protein layer being coupled to linker molecules that are bound to low molecular weight antigens. None of the paragraphs in Tao to which the Examiner refers to in the Official action discloses or suggests such a surface. What can be readout in those paragraphs and in the rest of the document as well is, however, that the protein is used as a captured ligand that will capture (bind to) directly or indirectly the analyte target, thus the protein is a part of the binding pair (binding ligand respectively target analyte) that will enable detection of the target analyte, which is not the case according to present claim 1. The "capture ligand" on the coated surface of claim 1 is the low molecular antigen not the protein layer. The low molecular antigens bound on the coated surface as defined in claim 1 will bind to antibodies with a specific affinity for these antigens and during a displacement reaction they will be displaced from the coated surface by the antigens in the test solution to which they have a higher affinity to and by measuring the weight loss from the coated surface the analyte in the test solution will be determined.

As discussed at the interview, Applicants' representative pointed out that the feature of only shorter aliphatic chains of less than 4 carbon atoms produces unexpected results of a significant displacement of antibody upon exposure to the analyte. Reference is made to page 8, last two paragraphs to page 9, first paragraph of the specification which discusses these advantages. Applicants also most respectfully direct the Examiner's attention to MPEP § 2145 wherein it is stated that Office personnel should consider all rebuttal argument and evidence presented by Applicants and the citation of In re Soni for error in not considering evidence presented in the specification.

Tao teaches both shorter and longer linkers, but does not teach the linker between the protein layer and an antigen and therefore the linker is in a different location and does not suggest the presently claimed invention to one of ordinary skill in the art. The Examiner noted at the interview that Applicants' arguments will be considered upon submission.

During the interview, Applicants' attorney reiterated the arguments already of record and that it was not possible to combine the references as suggested in the Official Action which was based upon hindsight reconstruction, based upon Applicants' disclosure. Applicants most respectfully directs the Examiner's attention to the present specification, at the bottom of page 8, wherein it is stated that a series of conjugates between cocaine derivatives, i.e. cocaine bound to linker molecules, and a protein, albumin, were made. Only the derivatives having shorter aliphatic chains than 4 carbon atoms in addition to possible carbon atoms in the functional end groups showed a significant displacement of antibodies on exposure to the analyte. See especially claims 12 and 16-19. Applicants most respectfully submit that this disclosure is evidence in terms of these tests that establishes the unique features of the presently claimed invention, unexpected results, due to the chain length as specified in the claim. The Examiner's attention is also must respectfully directed to MPEP § 2145 wherein it is stated that Office personnel should consider all rebuttal argument and evidence

presented by Applicants and the citation of In re Soni for error in not considering evidence presented in the specification.

At the interview, the Examiner pointed to the Tao et al reference as suggesting such short chained linkers but the undersigned pointed out that these do not correspond to the location in the presently claimed invention. The Examiner also referred to paragraph [0233] of the Tao reference for the teaching that the short chain linker was necessary so that minimal pertubations of a double stranded nucleic acid is effected. This relates to formation of double stranded nucleic acids containing electron transfer moieties (ETMs), page 3 paragraph [0036] but it is pointed out that this is not the same relationship as in the presently claimed invention as would be appreciated by one of ordinary skill in the art. It is further noted that the preferred embodiments included methylene, ethylene, ethylene glycol, propylene, and butylene and that there was nothing to suggest the unique results achieved by the presently claimed invention because of the specified linker required by the present invention. When the teachings of the references as a whole are considered, there is no rational basis to combine the teachings in the expectation of achieving the present claimed invention. Accordingly, in view of the above stated it would not be obvious to a person skilled in the art at all to modify the teachings of Miura et al. in view of Jacobs et al. and further in view of Tao et al. in order to arrive at the invention defined in present claim 1 as there are no incentives or suggestions pointing in that direction in any of the mentioned documents. Thus, present claim 1 is considered to be patentable in view of the prior art. Claims 2, 3, 5, 6, 12, 13 and 15-18 are patentable due to their dependency on independent claim 1. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 4 and 14 under 35 U.S.C. 103(a) as being unpatentable over Miura et al. in view of Jacobs et al. further in view of Tao et al., as applied to claim 1, further in view of Houser et al., has been carefully considered but is most respectfully traversed in view of the above comments. The Houser reference does not overcome the deficiencies of the primary references. Accordingly, it is most respectfully requested that this rejection be withdrawn.

In view of the above comments, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,
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